

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Faries MB, Thompson JF, Cochran AJ, et al. Completion dissection or observation for sentinel-node metastasis in melanoma. *N Engl J Med* 2017;376:2211-22. DOI: 10.1056/NEJMoa1613210

## Supplemental Appendix:

Supplement to: Faries, Thompson, Cochran, *et. al.* "Completion Dissection vs. Observation for Melanoma Sentinel Node Metastasis"

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**Trial Committees:**

Executive Committee: Donald L. Morton, MD, Mark B. Faries, MD, Alistair J. Cochran, MD, John F. Thompson, MD, Dave SB Hoon, PhD, David A. Elashoff, PhD, Robert Elashoff, PhD

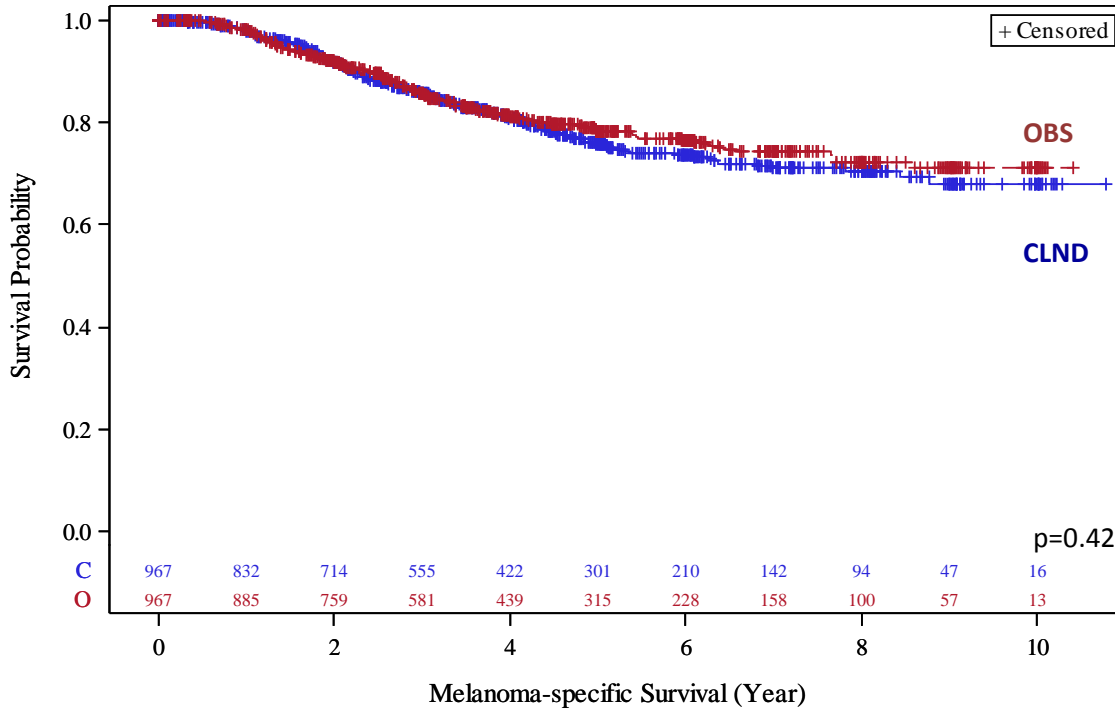
Data Safety Monitoring Board: Michael Mastrangelo, MD (Chair), Norman Beegun, Esq., Paul Chapman, MD, Daniel Coit, MD, Steven Piantadosi, MD, PhD, Bruce Turnbull, PhD, Marshall Urist, MD.

Pathology Oversight Committee: Alistair Cochran, MD, Richard Scolyer, MD, Martin Cook, MD, Hans Starz, MD, Roderick Turner, MD

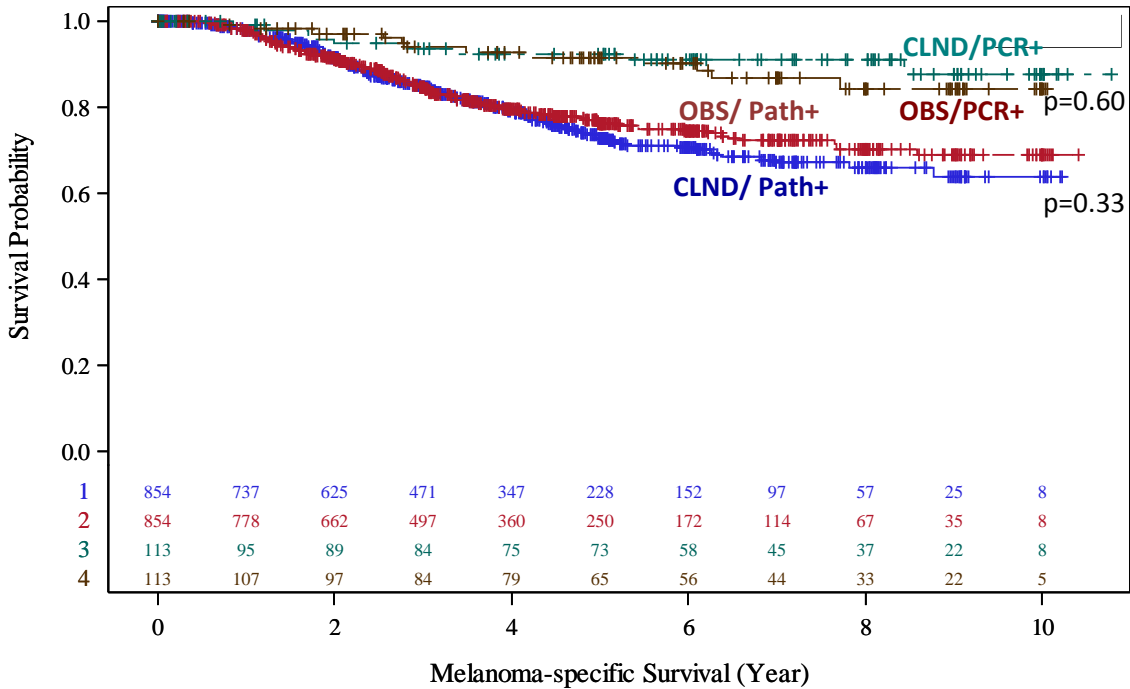
Ultrasound Oversight Committee: Roger Uren, MD, Vicky Schiller, MD, Edwin Glass, MD, Frank Roemer, MD, HJ Teertstra, MD

Clinical Trial Operations Center: Lisa Van Kreuningen, Paul Linke, Stacey Stern

**Figure S1a. Melanoma-specific Survival (Intent to treat)**

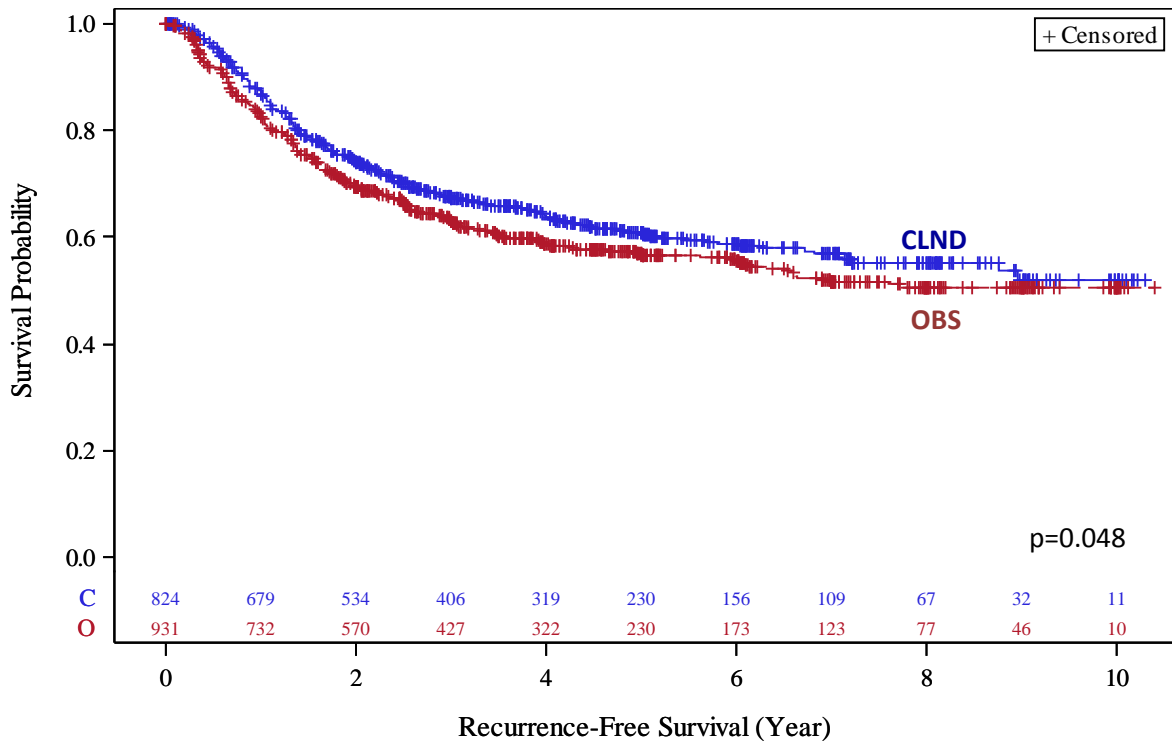


**Figure S1b. Melanoma-specific Survival (Intent to treat) by metastasis detection method**

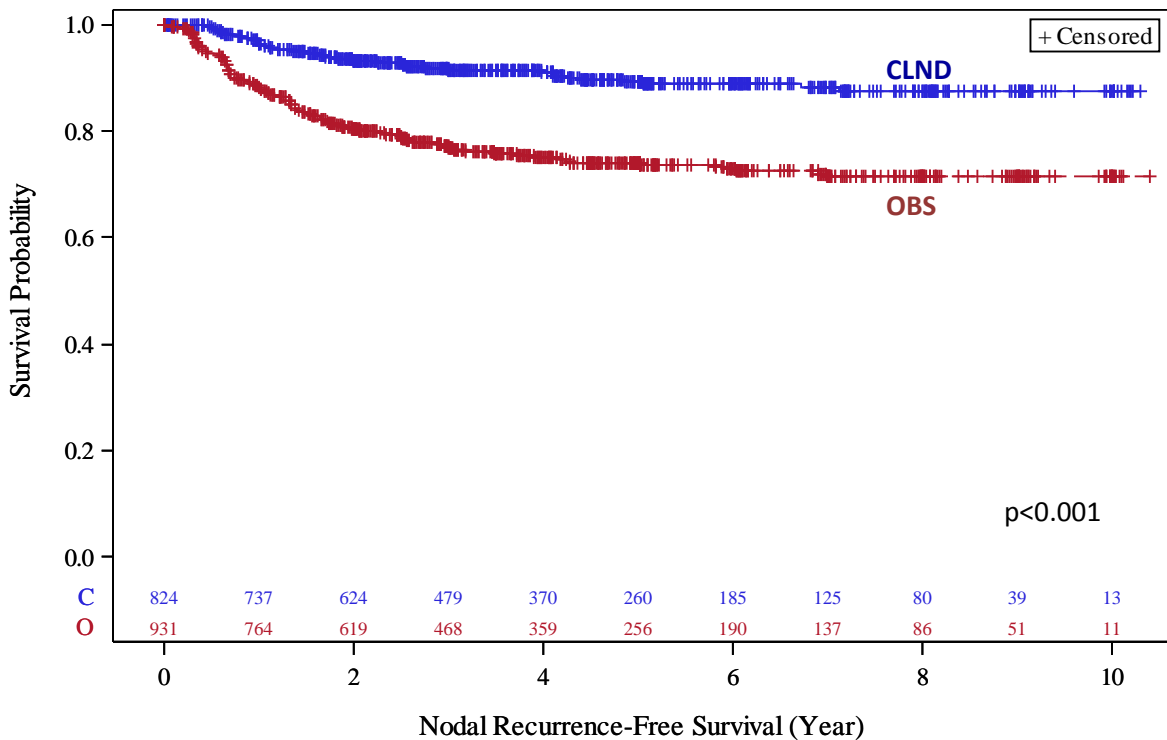


**Figure S1. a. Melanoma-specific survival (Intent to treat) b: Melanoma-specific survival by SLN metastasis detection method (Intent to treat). P-values are by the logrank test.**

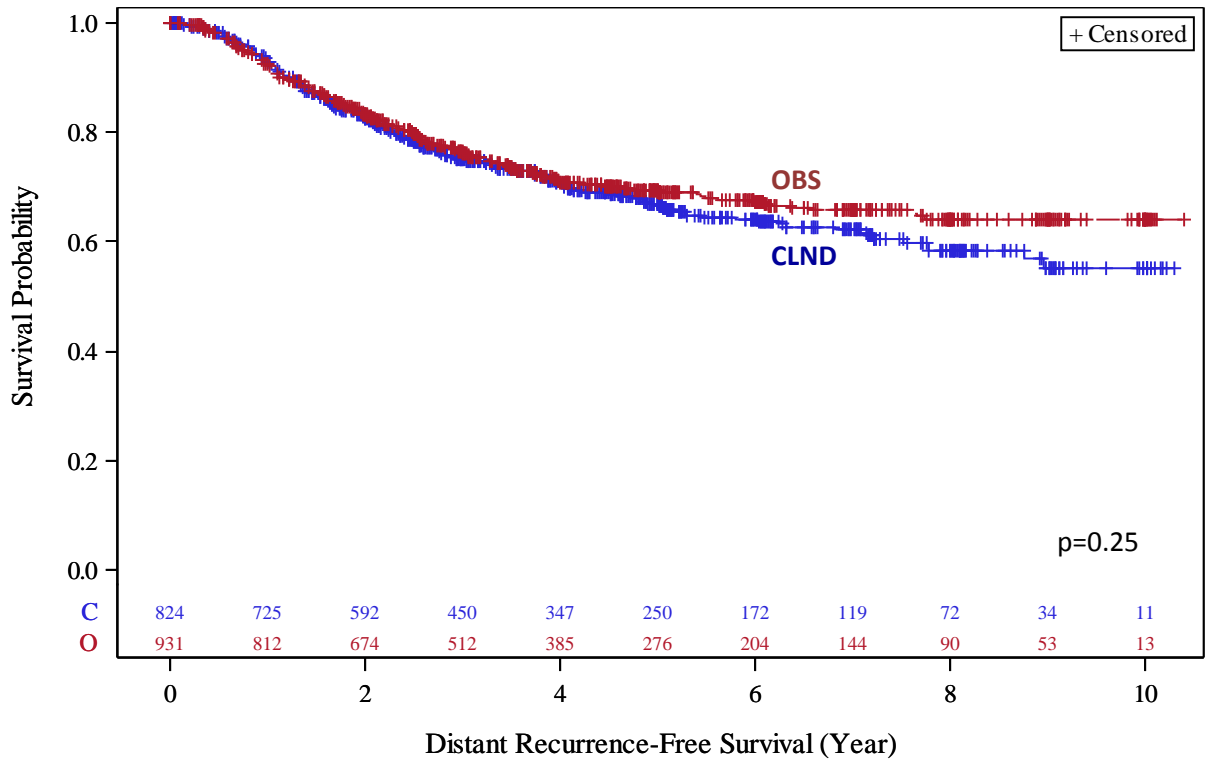
**Figure S2a. Disease-free survival (Pathology positive and RT-PCR positive combined.)**



**Figure S2b. Nodal disease-free survival (Pathology positive and RT-PCR positive combined.)**

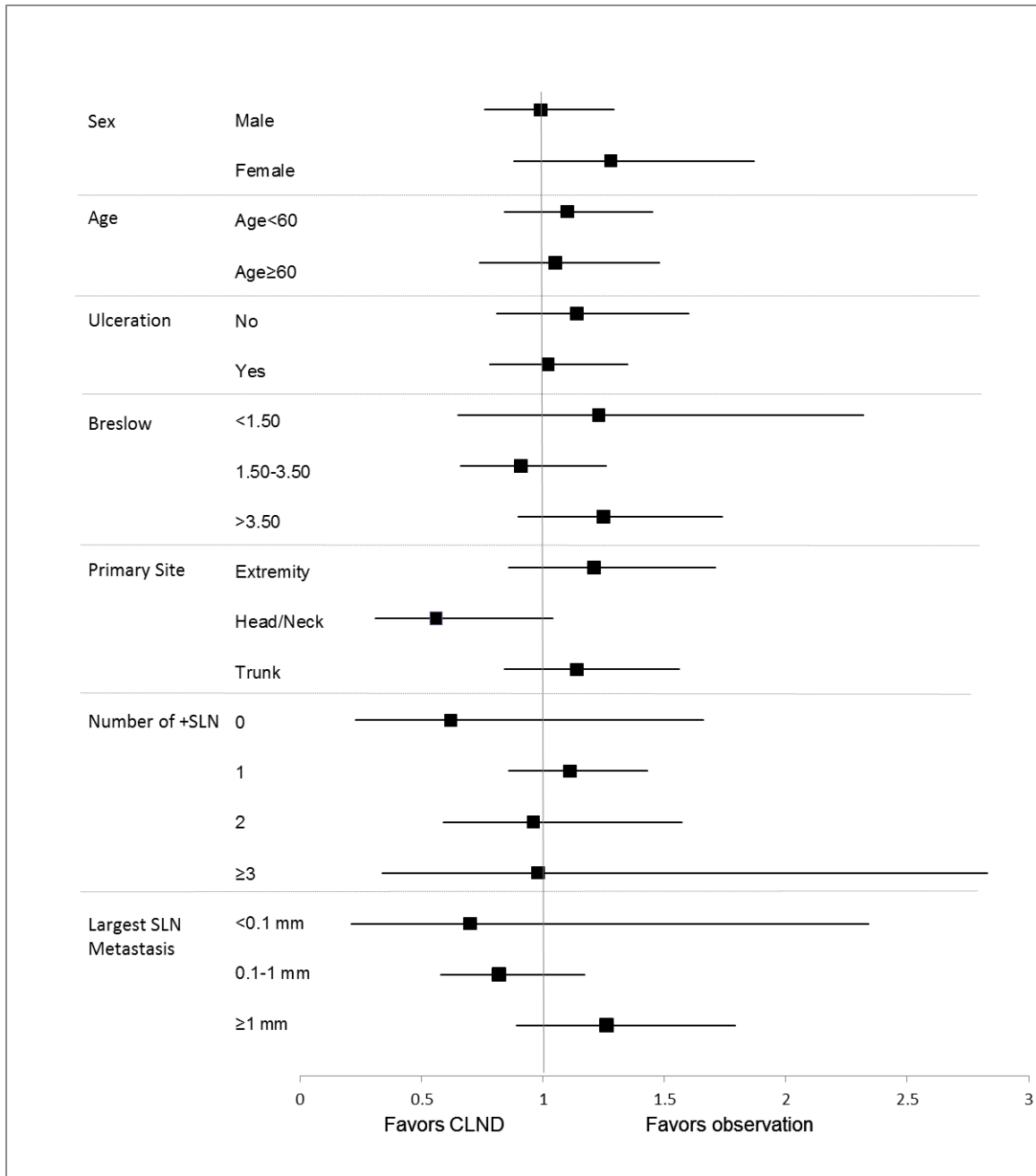


**Figure S2c.** Distant disease-free survival (Pathology positive and RT-PCR positive combined.)



**Figure S2.** a. Disease-free survival combining pathology and RT-PCR positive groups. b. Nodal disease-free survival combining pathology positive and RT-PCR positive) c. Distant disease-free survival combining pathology positive and RT-PCR positive) P-values are by the logrank test.

**Figure S3.** Forest plot of melanoma-specific survival hazard ratio by subgroups



**Figure S3:** Forest plot for melanoma-specific survival hazard ratio by subgroup (univariable)

**Table S1:** Trial subject demographics (Intent to treat)

<b>Table S1: Demographics (ITT)</b>			
<b>Characteristic</b>		<b>CLND N=967</b>	<b>Nodal OBS N=967</b>
Sex	Female	415 (43.0%)	399 (41.3%)
	Male	552 (57.0%)	568 (58.7%)
Age (years)			
	Mean $\pm$ SD	52.4 $\pm$ 13.1	52.9 $\pm$ 13.6
	Median, range	53.3, 18-76	54.5, 19-76
Smoking Status			
	Never	560 (59.3%)	549 (58.5%)
	Former	214 (22.7%)	230 (24.4%)
	Current	169 (18.0%)	162 (17.1%)
	[missing]	[24]	[26]
Breslow (mm)			
	Mean $\pm$ SD	2.75 $\pm$ 2.37	2.68 $\pm$ 2.10
	Median, range	2.10 (0.34 – 28.0)	2.10 (0.35 – 30.0)
	<1.50	280 (29.0%)	274 (28.3%)
	1.50 – 3.50	476 (49.2%)	476 (49.2%)
	>3.50	211 (21.8%)	217 (22.5%)
Primary Site			
	Extremity	394 (40.7%)	397 (41.1%)
	Head/Neck	132 (13.7%)	129 (13.3%)
	Trunk	441 (45.6%)	441 (45.6%)
Ulceration			
	Absent	609 (63.0%)	602 (62.3%)
	Present	358 (37.0%)	365 (37.7%)
# Positive SLN			
	0 (RT-PCR+)	113 (11.7%)	113 (11.7%)
	1	689 (71.2%)	670 (69.3%)
	2	137 (14.2%)	168 (17.4%)
	3	18 (1.9%)	11 (1.1%)
	>3	10 (1.0%)	5 (0.5%)
Mean SLN metastasis *		1.06mm	1.10mm
Median SLN metastasis *		0.59mm	0.67mm
Interquartile range		0.27-1.28 mm	0.22-1.38 mm
SLN metastasis size			
	<0.1mm	52	70
	0.1-1mm	379	352
	>1 mm	207	222
Received adjuvant therapy**		74 (8.1%)	63 (6.6%)

No significant difference between the CLND and Nodal observation groups for all factors.

\* SLN metastasis burden, longest diameter of largest focus, not available in 426.

\*\* Data not available in 69 subjects



**Table S2: Comparison of included/excluded subjects within CLND arm**

Characteristic		Included N=824	Excluded N=143	p-value
Sex	Female	346 (42.0%)	69 (42.0%)	NS
	Male	478 (58.0%)	74 (58.0%)	
Age (years)				NS
	Mean $\pm$ SD	52.5 $\pm$ 12.9	51.9 $\pm$ 13.8	
	Median, range	53.7, 18-76	51.7, 22-76	
Smoking Status				p=0.0241*
	Never smoked	463 (57.7%)	97 (69.3%)	
	Quit smoking	193 (24.0%)	21 (15.0%)	
	Smoking	147 (18.3%)	22(15.7%)	
	[missing]	[21]	[3]	
Breslow (mm)				NS
	Mean $\pm$ SD	2.76 $\pm$ 2.34	2.71 $\pm$ 2.53	
	Median, range	2.10 (0.34 – 28.0)	2.00 (0.50 – 23.0)	
	<1.50	237 (28.8%)	43 (30.1%)	
	1.50 – 3.50	404 (49.0%)	72 (50.3%)	
	>3.50	183 (22.2%)	28 (19.6%)	
Primary Site				NS
	Extremity	327 (39.7%)	67 (46.8%)	
	Head/Neck	113 (13.7%)	19 (13.3%)	
	Trunk	384 (46.6%)	57 (39.9%)	
Ulceration				p=0.0401*
	Absent	508 (61.7%)	101 (70.6%)	
	Present	316 (38.3%)	42 (20.4%)	
No. of Positive SLN				p<0.0001**
	0 (RT-PCR+)	80 (9.7%)	33 (23.1%)	
	1	596 (72.3%)	93 (65.0%)	
	2	121 (14.7%)	16 (11.2%)	
	3	18 (2.2%)	0 (0%)	
	>3	9 (1.1%)	1 (0.7%)	

\*Chi-square test \*\* Wilcoxon rank sum test

<b>Table S3. Assessment of prognostic factors including RT-PCR positive group</b>					
<b>Factors</b>		<b>CLND</b>		<b>OBS</b>	
		HR (95% CI)	P-value	HR (95% CI)	P-value
Sex	Male vs. Female	1.18 (0.84-1.66)	0.3459	1.48 (1.03-2.13)	0.0326
Age		1.00 (0.99-1.01)	0.9420	1.01 (0.99-1.02)	0.1783
Breslow(mm)	<1.50	1.00 (reference)		1.00 (reference)	
	1.50 - 3.50	1.61 (0.97-2.68)	0.0663	1.95 (1.15-3.31)	0.0135
	>3.50	3.72 (2.18-6.37)	<.0001	3.48 (2.00-6.06)	<.0001
Ulceration	present vs. absent	1.97 (1.41-2.75)	<.0001	2.26 (1.62-3.13)	<.0001
Primary site	Extremity	1.00 (reference)		1.00 (reference)	
	Head/neck	0.84 (0.48-1.47)	0.5451	1.54 (0.95-2.49)	0.0778
	Trunk	1.18 (0.85-1.65)	0.3269	1.07 (0.76-1.51)	0.6953
# of positive SN	0	1.00 (reference)		1.00 (reference)	
	1	2.62 (1.12-6.12)	0.0256	1.92 (1.03-3.60)	0.0408
	2	2.89 (1.18-7.12)	0.0208	2.48 (1.24-4.93)	0.0098
	≥3	3.19 (1.14-8.90)	0.0270	3.87 (1.33-11.3)	0.0133
Non-SLN (positive v. negative)		1.23 (1.13-1.34)	<.0001		

<b>Table S4 Initial recurrence types (Per protocol, Pathology positive)</b>			
<b>Recurrence status</b>	<b>CLND</b> (n=744)	<b>OBS</b> (n=820)	<b>Total</b> (n=1564)
Without recurrence	465	472	937
With recurrence(s)	279	348	627
Local-regional recurrence only	32	25	57
Nodal recurrence only	10	63	73
Distant recurrence only	128	84	212
Local-regional and Nodal	4	26	30
Local and distant recurrences	51	31	82
Nodal and distant recurrences	31	73	104
Local-regional, nodal and distant	23	46	69
With local-regional recurrence	110	128	238
With nodal recurrence	68	208	286
With distant recurrence	233	234	467

\* Local-regional recurrence includes satellite and in-transit metastases